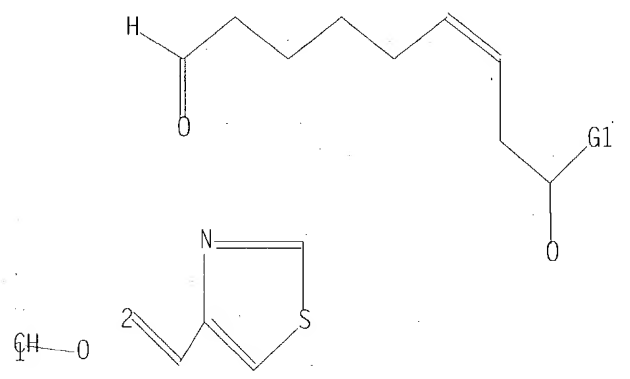
=> d his

(FILE 'HOME' ENTERED AT 12:23:18 ON 20 JUN 2004)

FILE 'REGISTRY' ENTERED AT 12:23:26 ON 20 JUN 2004
L1 STRUCTURE UPLOADED
L2 STRUCTURE UPLOADED
L3 1 S L1
L4 35 S L1 FULL
L5 1 S L2
L6 20 S L2 FULL

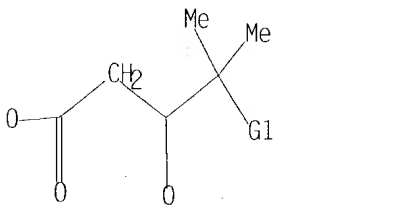
FILE 'CAPLUS' ENTERED AT 12:24:47 ON 20 JUN 2004
L7 18 S L4 AND L6

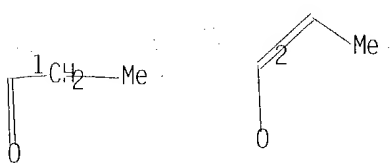
=> d que l7 stat
L1 STR



G1 [@1],[@2]

Structure attributes must be viewed using STN Express query preparation.
L2 STR



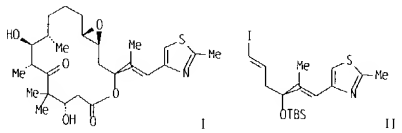


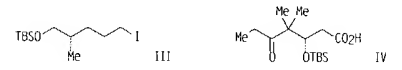
G1 [@1],[@2]

Structure attributes must be viewed using STN Express query preparation.
L4 35 SEA FILE=REGISTRY SSS FUL L1
L6 20 SEA FILE=REGISTRY SSS FUL L2
L7 18 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND L6

=> d 1-18 bib abs hitstr

L7 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:4456 CAPLUS
DN 138:237914
TI The total synthesis and biological assessment of trans-epothilone A
AU Altmann, Karl-Heinz; Bold, Guido; Caravatti, Giorgio; Denni, Donatienne; Florsheimer, Andreas; Schmidt, Alfred; Rihs, Grety; Wartmann, Markus
CS Corporate Research, Novartis Pharma AG, Switz.
SO Helvetica Chimica Acta (2002), 85(11), 4086-4110
CODEN: HCACAV; ISSN: 0018-019X
PB Verlag Helvetica Chimica Acta
DT Journal
LA English
OS CASREACT 138:237914
GI



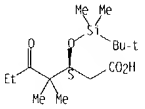


AB The total synthesis of (12S,13S)-trans-epothilone A (I) was achieved based on two different convergent strategies. In a first-generation approach, construction of the C(11)-C(12) bond by Pd0-catalyzed Negishi-type coupling between the C(12)-to-C(15) trans-vinyl iodide II and the C(7)-to-C(11) alkyl iodide III preceded the (nonselective) formation of the C(6)-C(7) bond by aldol reaction between the C(7)-to-C(15) aldehyde and the dianion derived from the C(1)-to-C(5) acid IV. The lack of selectivity in the aldol step was addressed in a second-generation approach, which involved construction of the C(6)-C(7) bond in a highly diastereoselective fashion through reaction between the acetonide-protected C(1)-to-C(6) diol ("Schinzer's ketone") and the C(7)-to-C(11) aldehyde. As part of this strategy, the C(11)-C(12) bond was established subsequent to the critical aldol step and was based on B-alkyl Suzuki coupling between the C(1)-to-C(11) fragment and C(12)-to-C(15) trans-vinyl iodide II. Both approaches converged at the

L7 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

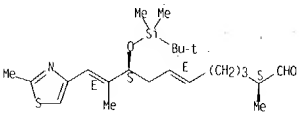
L7 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
stage of the 3-O, 7-O-bis-TBS-protected seco acid, which was converted to trans-deoxyepothilone A via Yamaguchi macrolactonization and subsequent deprotection. Stereoselective epoxidn. of the trans C(12)-C(13) bond could be achieved by epoxidn. with Oxone in the presence of the catalyst 1,2:4,5-di-O-isopropylidene-L-erythro-2,3-hexodiuro-2,6-pyranose, which provided a 8:1 mixt. of I and its (12R,13R)-epoxide isomer (V) in 27% yield (54% based on recovered starting material). The abs. configuration of I was established by X-ray crystallog. I is at least equipotent with natural epothilone A (VI) in its ability to induce tubulin polymn. and to inhibit the growth of human cancer cell lines in vitro. In contrast, the biol. activity of V is at least two orders of magnitude lower than that of VI or I.
IT 187283-45-0P 335160-10-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of trans-epothilone A and its ability to induce tubulin polymerization and growth inhibition of human carcinoma)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

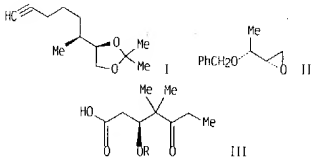


RN 335160-10-6 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6E,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



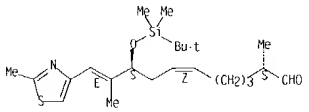
L7 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:674000 CAPLUS
DN 138:55771
TI Total synthesis of epothilone A through stereospecific epoxidation of the p-methoxybenzyl ether of epothilone C
AU Liu, Zhi-Yu; Chen, Ze-Cheng; Yu, Cheng-Zhi; Wang, Rui-Fang; Zhang, Ru-Zhou; Huang, Chu-Sheng; Yan, Zheng; Cao, De-Rong; Sun, Jian-Bo; Li, Gang
CS Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SO Chemistry--A European Journal (2002), 8(16), 3747-3756
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
OS CASREACT 138:55771
GI



AB The total synthesis of epothilone A is described by the coupling of four segments. Three of the segments, I, II and III (R = CH2-p-C6H4OMe), have only one chiral center; all other chiral centers were introduced by simple asym. catalytic reactions. The key steps are the ring opening of epoxide II with acetylide I for the construction of the C12-C13 cis double bond and a practical hydrolytic kinetic resolution (HKR) developed by Jacobsen group for the introduction the chiral center at C3. The stereospecific epoxidn. of 3-O-PMB epothilone C through long-range effect of 3-O-PMB protecting group gave high yields of the C12-C13 α-epoxide for the synthesis of target mol.
IT 188730-13-4P 327186-79-8P 331268-25-8P
331268-26-9P 331268-27-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone A from the coupling of three chiral fragments including the key steps of stereoselective epoxidn., epoxide opening, and hydrolytic kinetic resolution)
RN 188730-13-4 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

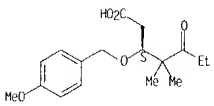
L7 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



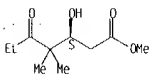
RN 327186-79-8 CAPLUS
CN Heptanoic acid, 3-[(4-methoxyphenyl)methoxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 331268-25-8 CAPLUS
CN Heptanoic acid, 3-hydroxy-4,4-dimethyl-5-oxo-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

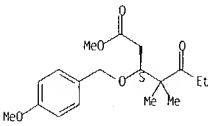
Absolute stereochemistry. Rotation (-).



RN 331268-26-9 CAPLUS
CN Heptanoic acid, 3-[(4-methoxyphenyl)methoxy]-4,4-dimethyl-5-oxo-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

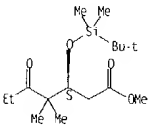
Absolute stereochemistry. Rotation (-).

L7 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



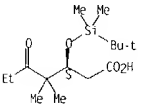
RN 331268-27-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 187283-45-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of epothilone A from the coupling of three chiral fragments including the key steps of stereoselective epoxidn., epoxide opening, and hydrolytic kinetic resolution)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

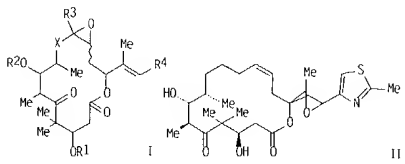
L7 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L7 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:655116 CAPLUS
DN 137:185358
TI Preparation of epothilone analogs as anticancer agents
IN Nicolaou, Kyriacos C.; He, Yun; Ninkovic, Sacha; Pastor, Joaquin; Roschangar, Frank; Sarabia, Francisco; Vallberg, Hans; Vourloumis, Dionisios; Winssinger, Nicolas; Yang, Zhen; King, N. Paul; Finlay, M. Ray
PA The Scripps Research Institute, USA
SO U.S., 160 pp., Cont.-in-part of U. S. Ser. No. 856,533, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6441186	B1	20020827	US 1997-923869	19970904
	WO 9825929	A1	19980618	WO 1997-EP7011	19971212
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9857577	A1	19980703	AU 1998-57577	19971212
	AU 746597	B2	20020502		
	EP 944634	A1	19990929	EP 1997-953808	19971212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9714140	A	20000229	BR 1997-14140	19971212
	CN 1246862	A	20000308	CN 1997-181771	19971212
	CN 1134443	B	20040114		
	JP 2001504856	T2	20010410	JP 1998-526247	19971212
	US 6380394	B1	20020430	US 1998-102602	19980622
PRAI	US 1996-32864P	P	19961213		
	US 1997-856533	B2	19970514		
	US 1997-923869	A2	19970904		
	WO 1997-EP7011	W	19971212		

OS MARPAT 137:185358
GI

L7 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



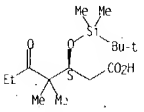
AB Epothilone A, epothilone B, analogs of epothilone and libraries of epothilone analogs of formula I [R1, R2 = H, silyl group, Me, Ac, PhCO, tert-butoxycarbonyl; R3 = H, Me, CHO, (substituted) CO2H, etc.; R4 = heterocyclyl, etc.; X = (CH2)n, n = 1-5] are synthesized. Epothilone A and B are known anticancer agents that derive their anticancer activity by the prevention of mitosis through the induction and stabilization of microtubulin assembly. Several of the analogs are demonstrated to have a superior cytotoxic activities as compared to epothilone A or epothilone B as demonstrated by their enhanced ability to induce the polymerization and stabilization of microtubules. Thus, epothilones A and B are prepared via olefin metathesis and macrocyclization. II was prepared and showed 7% tubulin polymerization

IT **187283-45-0P**
RL: CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone analogs as anticancer agents)

RN 187283-45-0 CAPLUS

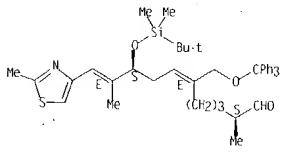
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **188730-13-4P 193146-27-9P 201136-70-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

L7 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



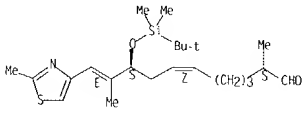
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(prepn. of epothilone analogs as anticancer agents)

RN 188730-13-4 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

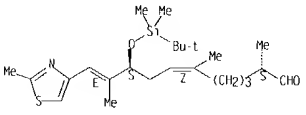
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193146-27-9 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 201136-70-1 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-6-[(triphenylmethoxy)methyl]-, (2S,6E,9S,10E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

L7 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:314889 CAPLUS

DN 136:340534

TI Method for the production of asymmetrically substituted acyloins and derivatives and for the production of epothilones B, D and their derivatives

IN Wessjohann, Ludger A.; Scheid, Guenther; Bornscheuer, Uwe; Henke, Erik; Kuit, Wouter; Orru, Romano

PA Morphochem A.-G., Germany

SO PCT Int. Appl., 182 pp.
CODEN: PIXXD2

DT Patent

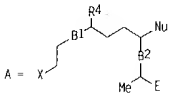
LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032844	A2	20020425	WO 2001-EP11992	20011016
	WO 2002032844	C1	20030821		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10051136	A1	20020418	DE 2000-10051136	20001016
	DE 10134172	A1	20030123	DE 2001-10134172	20010713
	AU 2002021693	A5	20020429	AU 2002-21693	20011016
	EP 1358144	A1	20031105	EP 2001-987736	20011016
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004082651	A1	20040429	US 2003-414510	20030415
PRAI	DE 2000-10051136	A	20001016		
	DE 2001-10134172	A	20010713		
	WO 2001-EP11992	W	20011016		

OS CASREACT 136:340534; MARPAT 136:340534

GI



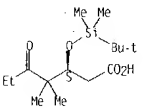
AB The invention relates to racemic and especially non-racemic acyloins, R1C(:O)CHR2OH [I; R1 = H, alkyl (especially Me, Et, Pr), aryl, alkylaryl,

L7 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CH2-aryl, (CH2)2-aryl, vinyl, alkynyl, propynyl, allyl, 3,3-dialkylallyl, C3-7-cycloalkyl, CHnF3-n, C3-7-oxacycloalkyl; R2 = alkyl, aryl, alkylaryl, CH2-aryl, (CH2)2-aryl, vinyl, alkynyl, propynyl, allyl, 3,3-dialkylallyl, E- or Z-haloalkenyl, 3,3-dihaloallyl, C3-7-cycloalkyl, CHnF3-n, C3-7-oxacycloalkyl, alkylpropynyl, 1-alkylallyl,3,3-dialkylallyl, A (joined at X); B1, B2 = single or E-, Z-, E/Z-double bond; B1 = epoxide; R4 = H, F, Cl, Br, I, alkyl (esp. Me, Et, CHnF3-n), aryl, alkylaryl, CH2-aryl, (CH2)2-aryl, vinyl, alkynyl, propynyl, allyl, 3,3-dialkylallyl, C3-7-cycloalkyl, CHnF3-n, C3-7-oxacycloalkyl; E = Me, CH2OH, CH2O-PG, CHO, CO2R, CO2-PG, CH2-halo, CONR2, CON(PG)2, CON(OMe)Me, CN; R = alkyl; Nu = R4, O-PG, OR, N(PG)2, N(alkyl)2, S-PG, S-alkyl, Se-PG, Se-alkyl, CN, N3, aryl, heteroaryl; PG = protective group], their derivs., a method for the prodn. thereof and the use of the same for producing epothilones and their derivs. The invention esp. relates to the prodn. of acyloins in a non-racemic form by means of diastereomer sepn. or synthesis using auxiliary agents and by means of enzymic resoln. of racemates. The invention also relates to epothilone synthesis components, a method for the prodn. thereof and the use of synthesis components for producing epothilones and their derivs. Thus, optically active (Z)-3-hydroxy-6,10-dimethyl-11-[(tert-butyldimethylsilyl)oxy]undeca-5,9-dien-2-one was prepd. from (±)-(Z)-3-acetoxy-6,10-dimethyl-11-[(tert-butyldimethylsilyl)oxy]undeca-5,9-dien-2-one via enzymic resoln. with Chirazyme L6. The optically active hydroxy ketone was converted to three 3-O-(tert-butyldimethylsilyl)epothilone D stereoisomers.

IT **187283-45-0P 415899-99-9P 415900-05-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of asym. substituted acyloins and derivs. for the of epothilone B, D and their derivs.)

RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

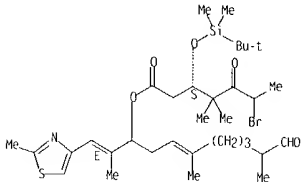
Absolute stereochemistry. Rotation (-).



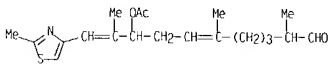
RN 415899-99-9 CAPLUS
CN Heptanoic acid, 6-bromo-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, 4,8-dimethyl-1-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-9-oxo-3-nonenyl ester, (3S)- (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



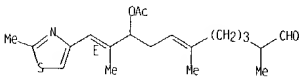
RN 415900-05-9 CAPLUS
CN 6,10-Undecadienal, 9-(acetyloxy)-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)- (9CI) (CA INDEX NAME)



IT **415900-24-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of asym. substituted acyloins and derivs. for the of epothilone B, D and their derivs.)

RN 415900-24-2 CAPLUS
CN 6,10-Undecadienal, 9-(acetyloxy)-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (10E)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



L7 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:293388 CAPLUS
DN 136:325359
TI Methods of preparing epothilones and related analogs
IN Avery, Mitchell A.
PA The University of Mississippi, USA
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002030356	A2	20020418	WO 2001-US32225	20011015
WO 2002030356	A3	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002013248	A5	20020422	AU 2002-13248	20011015
US 2002091269	A1	20020711	US 2001-981312	20011015
EP 1414384	A2	20040506	EP 2001-981618	20011015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
PRAI US 2000-240488P	P	20001013		
WO 2001-US32225	W	20011015		

OS MARPAT 136:325359
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

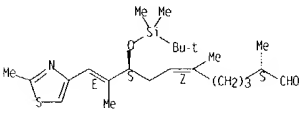
AB The present invention relates to methods for preparing epothilone analogs, such as I and II [R1 - R4 = H, alkyl, alkenyl, alkynyl, (substituted) aryl, cycloalkyl, heterocycle; R5 = H, PMB, DPS, TBS; R7 = H, TBS, TROC, CO(CH2)4Me; R8 = H, TBS], via an aldol condensation of III or IV [R6 = H, TBS, TMSM PMBM, SEM], with V, VI or VII (M = alkali metal) to form condensation product followed by macrolactonization. Thus, epothilone B II (R1-R4 = Me; R7-R8 = H) was prepared via a multistep synthesis starting from (R,R)-α-methyl-oxiranemethanol, 1-bromo-4-methyl-4-pentene, propyne and di-Et [(2-methylthiazol-4-yl)methane]phosphonate. The present invention also provides chemical compds., and methods for producing such chemical compds., that are useful in producing I and II.

IT **193146-27-9P 380605-84-5P 412926-48-8P**
412926-49-9P 412926-77-3P 412926-80-8P

L7 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
412927-00-5P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(methods for prepg. epothilone analogs and intermediates thereof)

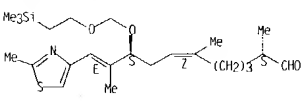
RN 193146-27-9 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



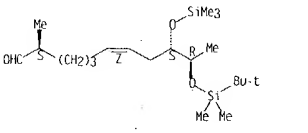
RN 380605-84-5 CAPLUS
CN 6,10-Undecadienal, 6,10-trimethyl-11-(2-methyl-4-thiazolyl)-9-[[2-(trimethylsilyl)ethoxy]methoxy]-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



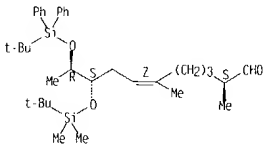
RN 412926-48-8 CAPLUS
CN 6-Undecenal, 10-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methyl-9-[(trimethylsilyl)oxy]-, (2S,6Z,9S,10R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



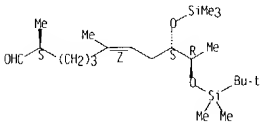
L7 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 412926-49-9 CAPLUS
CN 6-Undecenal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-10-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-2,6-dimethyl-, (2S,6Z,9S,10R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 412926-77-3 CAPLUS
CN 6-Undecenal, 10-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6-dimethyl-9-[(trimethylsilyl)oxy]-, (2S,6Z,9S,10R)- (9CI) (CA INDEX NAME)

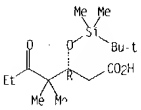
Absolute stereochemistry.
Double bond geometry as shown.



RN 412926-80-8 CAPLUS
CN 6-Undecenal, 10-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9-[(4-methoxyphenyl)methoxy]-2,6-dimethyl-, (2S,6Z,9S,10R)- (9CI) (CA INDEX NAME)

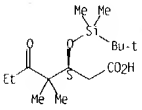
Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.

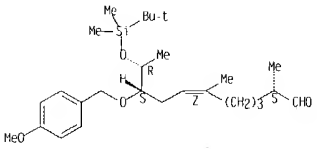


IT 187283-45-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(methods for preparing epothilone analogs and intermediates thereof)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

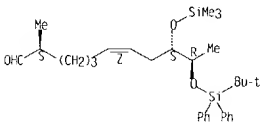


L7 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



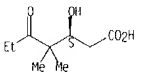
RN 412927-00-5 CAPLUS
CN 6-Undecenal, 10-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-2-methyl-9-[(trimethylsilyl)oxy]-, (2S,6Z,9S,10R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 188177-18-6 198571-87-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(methods for preparing epothilone analogs and intermediates thereof)
RN 188177-18-6 CAPLUS
CN Heptanoic acid, 3-hydroxy-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198571-87-8 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3R)- (9CI) (CA INDEX NAME)

L7 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:291687 CAPLUS
DN 136:325358
TI Procedure for the production of epothilone building blocks and synthesis of epothilone B, D and derivatives
IN Wessjohann, Ludger A.; Scheid, Guenther
PA Germany
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10051136	A1	20020418	DE 2000-10051136	20001016
WO 2002032844	A2	20020425	WO 2001-EP11992	20011016
WO 2002032844	C1	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002021693	A5	20020429	AU 2002-21693	20011016
EP 1358144	A1	20031105	EP 2001-987736	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004082651	A1	20040429	US 2003-414510	20030415
PRAI DE 2000-10051136	A	20001016		
DE 2001-10134172	A	20010713		
WO 2001-EP11992	W	20011016		

OS CASREACT 136:325358; MARPAT 136:325358
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention concerns 2 types of suitable building blocks for the synthesis of epothilones and their derivs., as well as precursors of these building blocks, such as R"COCH(CO2R)OC(:O)CH2X (X = H, OH, Cl, Br, I, O3SC6H4Me-4, O3SMe, O3SCF3, alkanoate, arylcarboxylate; R = H, alkyl, aryl alkylaryl, vinyl, CHnF3-n, C3-7-cycloalkyl, C3-7-oxacycloalkyl, H, Me, Et, Ph, CH2Ph; R" = R, especially Me). The invention further concerns the synthesis of these synthetic building blocks, whereby the synthetic building blocks are compds. with the general formula I [B1, B2, B3 = single or double bond (E, Z, E/Z mixture), epoxide, cyclopropane ring; E = Me, (un)protected CH2OH, CHO, CO2R, CH2X, CONR2, CONMeOMe, CN; EWG = E, CN, C(:O)R, dialkyl

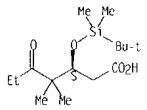
L7 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
phosphonate, SO2R, SO2OR, CF3, CCl3, NO2, R' = R, esp. H; Y = S, NH, NR, N-protecting group, O; Z = OH, O-PG, OR, :O, :N-Nu, :CH-heteroaryl, :CH-aryl, :PR3; Nu = R, O-PG, OR, N(PG)2, NR2, S-PG, SR, SeR, CN, N3, aryl, heteroaryl; dashed line = single or double bond; PG = protecting group] and Y'CH(B3Z')CR2COCHRX' [X' = OH, Cl, Br, I, O3SC6H4Me-4, O3SMe, O3SCF3, alkanoate, arylcarboxylate; Y' = H, OH, OR, O-PG, NH2, NR2, SR, SH, N(PG)2; Z' = :O, OH, OR, O-PG, NH2, :NH, NR2, :NR, :N-PG, N(PG)2, SR, S-PG, R]. The invention concerns furthermore the simple and repeated linkage of these synthetic building blocks to all open-chain and macrocyclic precursors, e.g., II [Y" = H, OH, OR, O-PG, NH2, NR2, N(PGp)2, SR, SH, Cl, Br, C(R')2-EWG] and III, of the epothilone and of its derived compds. The invention concerns these precursors as synthetic building blocks for epothilone analogs and in particular the synthesis of epothilones B and D and their derivs. from these precursors.

IT **187283-45-0P 412910-63-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone building blocks and synthesis of epothilone B, D and analogs and derivs.)

RN 187283-45-0 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

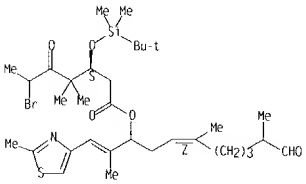


RN 412910-63-5 CAPLUS

CN Heptanoic acid, 6-bromo-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3Z)-4,8-dimethyl-1-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-9-oxo-3-nonenyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

L7 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

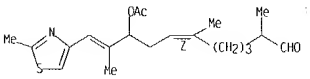


IT **412043-08-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of epothilone building blocks and synthesis of epothilone B, D and analogs and derivs.)

RN 412043-08-4 CAPLUS

CN 6,10-Undecadienal, 9-(acetyloxy)-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



L7 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:132141 CAPLUS

DN 136:318824

TI Synthetic and semisynthetic analogs of epothilones: chemistry and biological activity

AU Altmann, Karl-Heinz; Blommers, Marcel J. J.; Caravatti, Giorgio; Florsheimer, Andreas; Nicolaou, Kyriacos C.; O'Reilly, Terrence; Schmidt, Alfred; Schinzer, Dieter; Wartmann, Markus

CS TA Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.

SO ACS Symposium Series (2001), 796(Anticancer Agents), 112-130
CODEN: ACSMC8; ISSN: 0097-6156

PB American Chemical Society

DT Journal

LA English

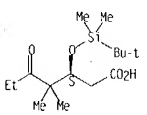
AB Epothilones A and B are naturally occurring microtubule depolymn. inhibitors, which exhibit potent in vitro antiproliferative activity. Epothilone B is a 3-30-fold more potent inhibitor of human cancer cell growth than paclitaxel in paclitaxel-sensitive cancer cell lines and in paclitaxel-resistant lines exceeds paclitaxel activity by 102 - 103-fold. In addition, epothilone B exhibits potent in vivo antitumor activity even in multidrug-resistant tumor models. In order to gain a better understanding of the structural requirements for epothilone-mediated cytotoxicity and antitumor activity and to discover analogs with similar potency but perhaps better tolerability in vivo, we have investigated a series of structural modifications involving the epoxide site (C12/C13) and the heterocyclic side-chain of epothilones. In this paper we present the synthesis of these analogs and we discuss the impact of such modifications on tubulin polymerization activity as well as cytotoxicity in vitro.

IT **187283-45-0P 335160-10-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic and semisynthetic analogs of epothilones and their chemical and biol. activity)

RN 187283-45-0 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

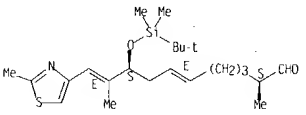


RN 335160-10-6 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6E,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L7 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



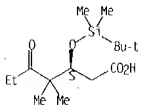
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:752384 CAPLUS
DN 136:37430
TI Total synthesis of epothilone B
AU Valluri, Muralikrishna; Hindupur, Rama M.; Bijoy, Panicker; Labadie, Guillermo; Jung, Jae-Chul; Avery, Mitchell A.
CS Department of Medicinal Chemistry School of Pharmacy Department of Chemistry and National Center for Natural Products Research, University of Mississippi, University, MS, 38677-1848, USA
SO Organic Letters (2001), 3(23), 3607-3609
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
OS CASREACT 136:37430
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A convergent and stereoselective total synthesis of epothilone B (I) is described. The key steps are Normant reaction, Wadsworth-Emmons reaction of a Me ketone II with the phosphonate reagent III, diastereoselective aldol condensation of aldehyde IV with enolate V to form the C6-C7 bond, and macrolactonization.
IT 187283-45-0 380605-84-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective total synthesis of epothilone B via Normant, Wadsworth-Emmons, diastereoselective aldol, and macrolactonization reactions)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

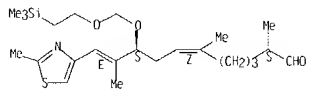
Absolute stereochemistry. Rotation (-).



RN 380605-84-5 CAPLUS
CN 6,10-Undecadienal, 2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-9-[[2-

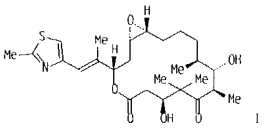
L7 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(trimethylsilyl)ethoxy]methoxy]-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

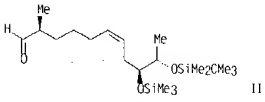


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

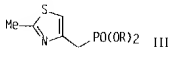
L7 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:708494 CAPLUS
DN 136:69672
TI Total synthesis of epothilone A
AU Hindupur, R. M.; Panicker, B.; Valluri, M.; Avery, M. A.
CS Department of Medicinal Chemistry, University of Mississippi, School of Pharmacy, University, MS, 38677-1848, USA
SO Tetrahedron Letters (2001), 42(42), 7341-7344
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 136:69672
GI



I



II

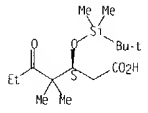


III

AB A convergent total synthesis of epothilone A (I) is described. The key steps are diastereoselective aldol condensation of aldehyde II to form the C6-C7 bond; macrolactonization and Wadsworth-Emmons reaction of Me ketone with phosphonate reagent III (R = Et).
IT 187283-45-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(total synthesis of epothilone A via stereoselective aldol, macrolactonization, and Wadsworth-Emmons reactions)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

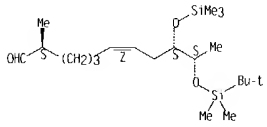
Absolute stereochemistry. Rotation (-).

L7 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



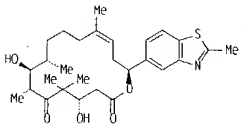
IT 383911-97-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilone A via stereoselective aldol, macrolactonization, and Wadsworth-Emmons reactions)
RN 383911-97-5 CAPLUS
CN 6-Undecenal, 10-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methyl-9-[(trimethylsilyl)oxy]-, (2S,6Z,9S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:138738 CAPLUS
DN 134:311010
TI Synthetic epothilone analogs with modifications in the northern hemisphere and the heterocyclic side-chain-synthesis and biological evaluation
AU End, Nicole; Bold, Guido; Caravatti, Giorgio; Wartmann, Markus; Altmann, Karl-Heinz
CS TA Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SO Proceedings of ECSOC-3, [and] Proceedings of ECSOC-4, Sept. 1-30, 1999 and 2000 (2000), Meeting Date 1999-2000, 1431-1442, Editor(s): Pombo-Villar, Esteban, Publisher: Molecular Diversity Preservation International, Basel, Switz.
CODEN: 69AXZT
DT Conference; (computer optical disk)
LA English
OS CASREACT 134:311010
GI

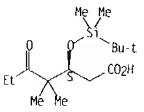


I

AB The authors have synthesized epothilone analogs, e.g. I, with modifications in the northern hemisphere and the heterocyclic side-chain. In all three cases the key steps for construction of the macrocyclic skeleton involve Yamaguchi macrolactonization, the build-up of the requisite seco-acid through aldol reaction between the C7-C15 aldehyde and the dianion of the O-protected C1-C6 β-hydroxy acid fragment, and the assembly of the C7-C15 aldehyde through the appropriate type of Pd(0)-catalyzed coupling reaction. The IC50 for growth inhibition of the KB-31 tumor cell line for I was 0.45 nM.
IT **187283-45-0 188177-18-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthetic epothilone analogs with modifications in the northern hemisphere and the heterocyclic side-chain-synthesis and biol. evaluation)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

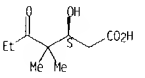
L7 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L7 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).



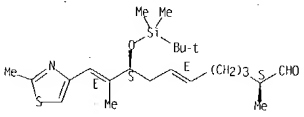
RN 188177-18-6 CAPLUS
CN Heptanoic acid, 3-hydroxy-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **335160-10-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic epothilone analogs with modifications in the northern hemisphere and the heterocyclic side-chain-synthesis and biol. evaluation)
RN 335160-10-6 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6E,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



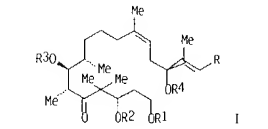
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:753225 CAPLUS
DN 132:3284
TI Preparation of intermediates for the synthesis of epothilones
IN Altmann, Karl-heinz; Bauer, Armin; Schinzer, Dieter
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

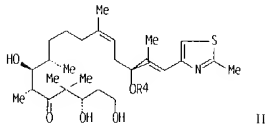
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959985	A1	19991125	WO 1999-EP3354	19990514
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9942622	A1	19991206	AU 1999-42622	19990514
	EP 1080082	A1	20010307	EP 1999-952092	19990514
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	US 6350878	B1	20020226	US 2000-715674	20001117
PRAI	GB 1998-10659	A	19980518		
	WO 1999-EP3354	W	19990514		
	WO 1999-EP5354	A1	19990514		

OS MARPAT 132:3284
GI

L7 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I



II

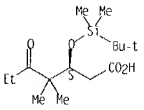
AB Epothilone B intermediates, such as I [R = heterocyclyl; R1, R2, R3, R4 = H, alc. protecting groups] were prepared. Thus, epothilone intermediate II (R4 = SiMe2CMe3) was prepared in a multistep synthetic sequence from starting materials such as 5-(benzyloxy)pentanoic acid, thioacetamide, 1,3-dichloroacetone, (5S)-(2,2-cyclohexylidenyl-4-oxo-1,3-dioxolan-5-yl)acetic acid, etc.

IT **187283-45-0P 193146-27-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of intermediates for the synthesis of epothilones)

RN 187283-45-0 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

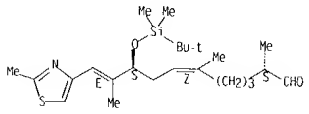


RN 193146-27-9 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX

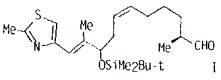
L7 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

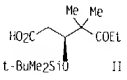


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:733552 CAPLUS
DN 132:107804
TI The formal total synthesis of epothilone A
AU Kalesse, Markus; Quitschalle, Monika; Claus, Eckhard; Gerlach, Kai; Pahl, Axel; Meyer, Hartmut H.
CS Institut Organische Chemie, Univ. Hannover, Hannover, D-30167, Germany
SO European Journal of Organic Chemistry (1999), (11), 2817-2823
CODEN: EJOCFK; ISSN: 1434-193X
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
OS CASREACT 132:107804
GI



I



II

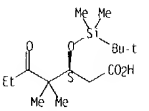
AB The formal total synthesis of epothilone A is described. The key steps in the synthesis of the northern hemisphere are a Z-selective 10-membered ring-closing metathesis (RCM) and the diastereoselective alkylation at C(8). Aldehyde I is formed by introduction of the thiazole moiety by a Wittig reaction and subsequent functional group transformation. An efficient route to keto acid II is described.

IT **187283-45-0P 188730-13-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(formal total synthesis of epothilone A)

RN 187283-45-0 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

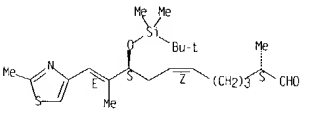


RN 188730-13-4 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L7 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:126888 CAPLUS

DN 130:196529

TI Preparation of new epothilone derivatives as pharmaceutical agents

IN Klar, Ulrich; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael

PA Schering Aktiengesellschaft, Germany

SO PCT Int. Appl., 185 pp.
CODEN: PIXXD2

DT Patent

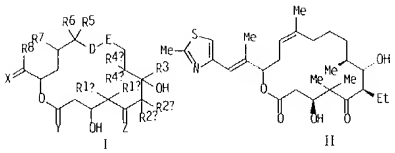
LA German

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9907692	A2	19990218	WO 1998-EP5064	19980810
	WO 9907692	A3	19990514		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19735574	A1	19990211	DE 1997-19735574	19970809
	DE 19735575	A1	19990211	DE 1997-19735575	19970809
	DE 19735578	A1	19990211	DE 1997-19735578	19970809
	DE 19748928	A1	19990429	DE 1997-19748928	19971024
	DE 19749717	A1	19990506	DE 1997-19749717	19971031
	DE 19751200	A1	19990520	DE 1997-19751200	19971113
	DE 19813821	A1	19990923	DE 1998-19813821	19980320
	AU 9893409	A1	19990301	AU 1998-93409	19980810
	EP 1005465	A2	20000607	EP 1998-946309	19980810
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001512723	T2	20010828	JP 2000-506196	19980810
	ZA 9810403	A	20000515	ZA 1998-10403	19981113
	US 2003144523	A1	20030731	US 2000-485292	20000503
PRAI	DE 1997-19735574	A	19970809		
	DE 1997-19735575	A	19970809		
	DE 1997-19735578	A	19970809		
	DE 1997-19748928	A	19971024		
	DE 1997-19749717	A	19971031		
	DE 1997-19751200	A	19971113		
	DE 1998-19813821	A	19980320		
	WO 1998-EP5064	W	19980810		

OS MARPAT 130:196529

GI



I II

AB Epothilone derivs. of formula I [X = O, alkylene-α,ω-dioxy, two alkoxy groups, etc.; Y = O, H2; Z = O, (H, OH), (H, protected OH); R1a, R1b = H, alkyl, aryl, aralkyl, or together = (CH2)m where m = 2, 3, 4, 5; R2a, R2b = H, alkyl, aryl, aralkyl, or together = (CH2)n where n = 2, 3, 4, 5; when D-E = CH2CH2 or when Y = O, R2a or R2b may not be H/Me; R3 = H, alkyl, aryl, aralkyl; R4a, R4b = H, alkyl, aryl, aralkyl, or together = (CH2)p where p = 2, 3, 4, 5; D-E = CH2CH2, CH:CH, C.tplbond.C, 2,3-oxiranediyl, CH(OH)CH(OH), CH(OH)CH2; R5 = H, alkyl, aryl, aralkyl; R6, R7 = H, together = a saturated bond or O; R8 = H, alkyl, aryl, aralkyl all of which may be substituted] are prepared. Thus, the title compds. (4S,7R,8S,9S,13E,16S(E))- and (4S,7R,8S,9S,13Z,16S(E))-4,8-dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethylcyclohexadec-13-en-2,6-dione (II) were prepared in many steps. The new compds. interact with tubulin by stabilizing formed microtubuli. They are capable of influencing cell division in a phase-specific manner and are suitable for the treatment of malignant tumors, such as ovarian, gastric, colon, breast, lung, head and neck carcinoma, adenocarcinoma, malignant melanoma, and acute lymphocytic and myelocytic leukemia. They are also suited for anti-angiogenesis therapy and for the treatment of chronic inflammatory diseases (psoriasis, arthritis). To prevent uncontrolled cell growth on, and for better tolerability of, medical implants, the derivs. can be introduced into or applied to polymeric materials. The compds. provided for in the invention can be used alone or, to achieve additive or synergistic effects, in combination with other principles and substance categories used in tumor therapy.

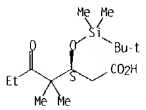
IT **187283-45-0P 190370-04-8P 198571-87-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone derivs. as antitumor agents)

RN 187283-45-0 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

L7 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

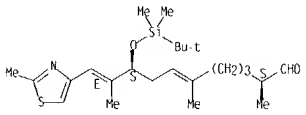
Absolute stereochemistry. Rotation (-).



RN 190370-04-8 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,9S,10E)- (9CI) (CA INDEX NAME)

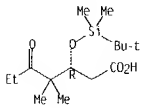
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 198571-87-8 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:405952 CAPLUS

DN 129:81625

TI Preparation of epothilone analogs as anticancer agents

IN Nicolaou, Costa Kyriacos; He, Yun; Ninkovic, Sacha; Pastor, Joaquin; Roschangar, Frank; Sarabia, Francisco; Vallberg, Hans; Vourloumis, Dionisios; Winssinger, Nicolas; Yang, Zhen; King, Nigel Paul; et al.

PA Novartis A.-G., Switz.; Scripps Research Institute

SO PCT Int. Appl., 213 pp.
CODEN: PIXXD2

DT Patent

LA English

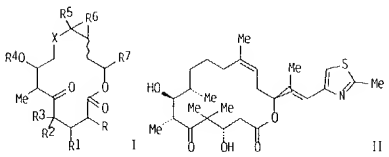
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9825929	A1	19980618	WO 1997-EP7011	19971212
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6441186	B1	20020827	US 1997-923869	19970904
	AU 9857577	A1	19980703	AU 1998-57577	19971212
	AU 746597	B2	20020502		
	EP 944634	A1	19990929	EP 1997-953808	19971212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9714140	A	20000229	BR 1997-14140	19971212
	JP 2001504856	T2	20010410	JP 1998-526247	19971212
	US 6660758	B1	20031209	US 1999-319885	19990924
PRAI	US 1996-32864P	P	19961213		
	US 1997-856533	A	19970514		
	US 1997-923869	A2	19970904		
	WO 1997-EP7011	W	19971212		

OS MARPAT 129:81625

GI

L7 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I II

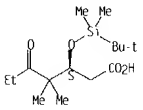
AB Epothilone A, epothilone B, analogs of epothilone and libraries of epothilone analogs of formula I [X = (CH2)n; n = 1-5; R1 = OH, OMe, absent; R2, R3 = H, CH2, Me; R4 = H, Me, protecting group; R5 = H, Me, CHO, (substituted) CO2H, etc.; R6 = O, CH2, absent; R7 = thiazolealkyl, etc.] are synthesized. Epothilone A and B are known anticancer agents that derive their anticancer activity by the prevention of mitosis through the induction and stabilization of microtubulin assembly. Several of the analogs are demonstrated to have a superior cytotoxic activity as compared to epothilone A or epothilone B as demonstrated by their enhanced ability to induce the polymerization and stabilization of microtubules. Thus, II was prepared and was shown to induce tubulin polymerization at 94% relative to GTP, and inhibit carcinoma cell growth.

IT **187283-45-0P 188730-13-4P 193146-27-9P**
201136-70-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone analogs as anticancer agents)

RN 187283-45-0 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

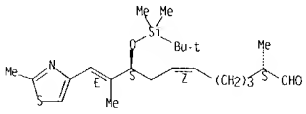


RN 188730-13-4 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

L7 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

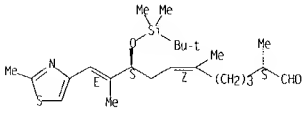
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193146-27-9 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

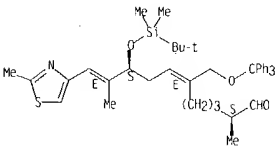


RN 201136-70-1 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-6-[(triphenylmethoxy)methyl]-, (2S,6E,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

L7 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:724919 CAPLUS

DN 127:346221

TI Synthesis of epothilones A and B in solid and solution phase. [Erratum to document cited in CA127:4950]

AU Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E.

CS Dep. Chemistry, Skaggs Inst. Chem. Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA

SO Nature (London) (1997), 390(6655), 100
CODEN: NATUAS; ISSN: 0028-0836

PB Macmillan Magazines

DT Journal

LA English

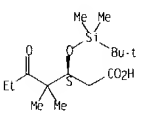
AB Reference 19, includes, in addition to a total synthesis of epothilone B, biol. data for compound 23 and other congeners similar to the reported in the Letter.

IT **187283-45-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of epothilone A and solution-phase synthesis of epothilone B (Erratum))

RN 187283-45-0 CAPLUS

CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



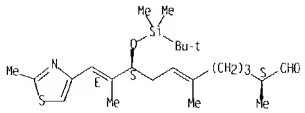
IT **190370-04-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of epothilone A and solution-phase synthesis of epothilone B (Erratum))

RN 190370-04-8 CAPLUS

CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

L7 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

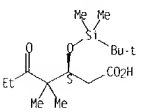


L7 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:528753 CAPLUS
DN 127:135660
TI Total Syntheses of Epothilones A and B via a Macrolactonization-Based Strategy
AU Nicolaou, K. C.; Ninkovic, S.; Sarabia, F.; Vourloumis, D.; He, Y.; Vallberg, H.; Finlay, M. R. V.; Yang, Z.
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, La Jolla, CA, 92037, USA
SO Journal of the American Chemical Society (1997), 119(34), 7974-7991
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 127:135660
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

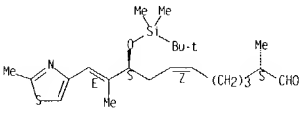
AB The total syntheses of epothilones A (I) (R = H) and B I (R = Me) and several analogs are described. The reported strategy relies on a macrolactonization approach and features selective epoxidn. of the macrocycle double bond in precursors II (R = H, Me) as well as high convergency and flexibility. Building blocks (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H, (S)-Me3CMe2SiOCH2CH(Me)CH2CH2CH2COR (R = H, Me), (III) [R2 = CH2CH2P+(Ph)3I-; CH2CHO] were constructed by asym. processes and coupled via Wittig, aldol, and macrolactonization reactions to afford the basic skeleton of epothilones and that of several of their analogs by a relatively short route. The utilization of intermediate III [R2 = (E)-CH2CH=C(Me)CH2CH2CH2I], obtained via a stereoselective Wittig reaction and its Enders coupling to SAMP hydrazone, in combination with a stereoselective aldol reaction with the modified substrate (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CH2OSiMe2CMe3 improved the stereoselectivity and efficiency of the total synthesis of these new and highly potent microtubule binding antitumor agents.
IT **187283-45-0P 188730-13-4P 190370-04-8P**
193146-27-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total syntheses of epothilones A and B via a macrolactonization-based strategy)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

L7 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).



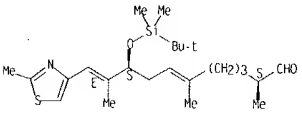
RN 188730-13-4 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 190370-04-8 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,9S,10E)- (9CI) (CA INDEX NAME)

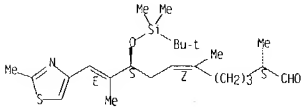
Absolute stereochemistry.
Double bond geometry as described by E or Z.



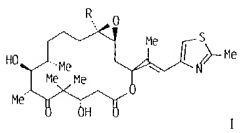
RN 193146-27-9 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

L7 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L7 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:330310 CAPLUS
DN 127:4950
TI Synthesis of epothilones A and B in solid and solution phase
AU Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E.
CS Dep. Chemistry, Skaggs Inst. Chem. Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Nature (London) (1997), 387(6630), 268-272
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
OS CASREACT 127:4950
GI

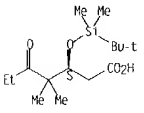


I

AB Epothilones A (I; R = H) and B (I; R = Me), two compds. that were recently isolated from myxobacterium Sorangium cellulosum strain 90, have generated intense interest among chemists, biologists and clinicians owing to the structural complexity, unusual mechanism of interaction with microtubules and anticancer potential of these mols. Like taxol, they exhibit cytotoxicity against tumor cells by inducing microtubule assembly and stabilization, even in taxol-resistant cell lines. Following the structural elucidation of these mols. by X-ray crystallog. in 1996, several synthesis of epothilones A and B have been reported, indicative of the potential importance of these mols. in the cancer field. Here we report the first solid-phase synthesis of epothilone A, the total synthesis of epothilone B, and the generation of a small epothilone library. The solid-phase synthesis applied here to epothilone A could open up new possibilities in natural-product synthesis and, together with solution-phase synthesis of other epothilones, paves the way for the generation of large combinatorial libraries of these important mols. for biol. screening.
IT **187283-45-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of

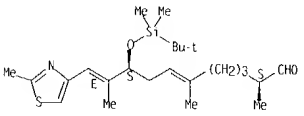
L7 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
epothilone A and soln.-phase synthesis of epothilone B)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



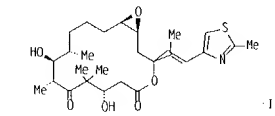
IT **190370-04-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of epothilone A and solution-phase synthesis of epothilone B)
RN 190370-04-8 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6,10-trimethyl-11-(2-methyl-4-thiazolyl)-, (2S,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:206419 CAPLUS
DN 126:251010
TI Total synthesis of epothilone A: the macrolactonization approach
AU Nicolaou, K. C.; Sarabia, Francisco; Ninkovic, Sacha; Yang, Zhen
CS Dep. Chem., Skaggs Inst. Chem. Biol., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Angewandte Chemie, International Edition in English (1997), 36(5), 525-527
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 126:251010
GI



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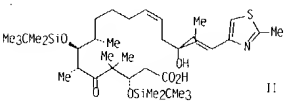
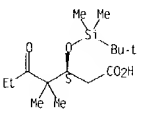


II

AB Epothilone A (I) was prepared via a highly convergent and flexible route with macrolactonization of hydroxy acid II as the key step.
IT **187283-45-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(total synthesis of epothilone A via a macrolactonization approach)
RN 187283-45-0 CAPLUS
CN Heptanoic acid, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,4-dimethyl-5-oxo-, (3S)- (9CI) (CA INDEX NAME)

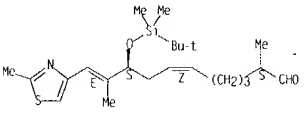
Absolute stereochemistry. Rotation (-).



L7 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **188730-13-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilone A via a macrolactonization approach)
RN 188730-13-4 CAPLUS
CN 6,10-Undecadienal, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10-dimethyl-11-(2-methyl-4-thiazolyl)-, (2S,6Z,9S,10E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT